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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/774,681	02/01/2001	Linda A. Sherman	313332000101	3045
21874	7590	10/11/2005		
EDWARDS & ANGELL, LLP P.O. BOX 55874 BOSTON, MA 02205			EXAMINER SCHWADRON, RONALD B	
			ART UNIT	PAPER NUMBER
			1644	
DATE MAILED: 10/11/2005				

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/774,681

**Applicant(s)**

SHERMAN ET AL.

**Examiner**

Ron Schwadron, Ph.D.

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 6-31 is/are pending in the application.
- 4a) Of the above claim(s) 20 and 21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 6-19 and 22-31 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_.

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1. Applicant's election with traverse of the species elected in the reply filed on 5/12/2003 is acknowledged. The traversal is on the ground(s) that are stated. This is not found persuasive because the searching of additional species would place an undue burden on the Examiner.

The requirement is still deemed proper and is therefore made FINAL.

2. The previously pending rejections are withdrawn in view of applicants arguments and the amended claims.

3. Applicant needs to update the status of all US applications disclosed in the specification.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 6,9-12,15-19,22-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed for the recitation of "transmembrane and cytoplasmic region of a CD3, CD8 or CD16 receptor" in claim 6 or 11 or 18. Regarding applicants comments, the cited passage of the specification discloses use of zeta regions of the CD3, CD8 or CD16 receptor, but does not disclose the scope of the claimed invention which encompasses use of portions of said molecules other than the zeta region.

There is no support in the specification as originally filed for the scope of claims 24-28. Applicant has indicated that said claims find support in Figure 1. Regarding claim 24, Figure 1 discloses a variety of specific constructs. However, the claimed nucleic

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acid encompasses constructs not depicted in said Figure. The claimed nucleic is broader in scope than said disclosure because it lacks the leader sequence, it doesn't specify that the variable region is attached to the transmembrane portion of the zeta chain, and it encompasses other attached molecules or amino acids because of the use of comprising language. Regarding claim 25, the claimed nucleic is broader in scope than said disclosure because it lacks the leader sequence, it doesn't specify that the variable region is attached to the transmembrane portion of the zeta chain, and it encompasses other attached molecules or amino acids because of the use of comprising language. Regarding claim 26, Figure 1 shows a CD8 hinge inserted into a particular region of the construct whilst the claim encompasses a CD 8 hinge that is inserted other than in said location.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 6-10,15-19,23,28-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mule (WO 95/06409) in view of Sette et al.

Mule teaches a nucleic acid encoding a TCR alpha and beta chain which binds a tumor antigen wherein the construct also includes the  $\zeta$  region of CD3 (see claims 1-3,8,13, page 16, penultimate paragraph) wherein claim 8 encompasses the molecule of claim 2. Mule teach expression vectors encoding nucleic acids comprising a leader sequence and said TCR, and T cells containing said vectors and methods of making the aforementioned (see page 14-16). Human CD3 is known in the art. Mule teaches single chain TCR (see page 15, second paragraph). Mule does not teach use of a nonhuman TCR which is HLA A2 restricted. Mule discloses that the TCR can be derived from known CTL (see page 15, second paragraph). Sette et al. disclose the use of HLA A2 transgenic mice that produce T cells with nonhuman TCR that are HLA A2 restricted (see page 5588, second column). Said system has the advantage that T cells can be produced by immunizing mice using methods not acceptable in humans (for example immunization of antigen with IFA used in the example, page 5587, second column). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Mule teaches the claimed invention except for use of nonhuman TCR, whilst methods of generating nonhuman TCR that were HLA A2 restricted were known in the art. One of ordinary skill in the art would have been motivated to do the aforementioned because Mule discloses that the TCR can be derived from known CTL.

8. Claims 11-14 rejected under 35 U.S.C. 103(a) as being unpatentable over Mule (WO 95/06409) in view of Sette et al. as applied to claims 6-10,15-19,23,28-31 above, and further in view of Reinherz et al. (US Patent 6,416,971).

The previous rejection renders obvious the claimed invention except for use of a flexible linker such as that of claim 12. Reinherz et al. teaches a flexible linker encompassed by that recited in claim 12 and the advantages of using such a linker to connect the alpha and beta chains of a TCR construct (see column 4, penultimate paragraph). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Mule teaches the claimed invention except for use of a flexible linker such as that of claim 12 whilst Reinherz et al. teaches a flexible linker encompassed by that recited in claim 12 and the

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advantages of using such a linker to connect the alpha and beta chains of a TCR construct.

9. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mule (WO 95/06409) in view of Sette et al. as applied to claims 6-10,15-19,23,28-31 above, and further in view of Disis et al.

The previous rejection renders obvious the claimed invention except wherein the tumor associated antigen is Her2/neu. Mule teaches that the TCR used can recognize cancer cells (see page 16, penultimate paragraph). Disis et al. teach that HER-2/neu is a cancer cell antigen recognized by T cells. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the previous rejection renders obvious the claimed invention except wherein the tumor associated antigen is Her2/neu, Mule teaches that the TCR used can recognize cancer cells whilst Disis et al. teach that HER-2/neu is a cancer cell antigen recognized by T cells.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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RONALD B. SCHWADRON  
PRIMARY EXAMINER  
GROUP ~~1800~~ 1644

Ron Schwadron, Ph.D.

Primary Examiner

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